

**In the Specification:**

Please replace the paragraph beginning at page 6, line 6 with the following:

--**Figure 1.** Preliminary CLASP-5 cDNA sequence (SEQ ID NO:3; amino acid sequences = SEQ ID NOS:4 and 5). Notable protein motifs are labeled above the nucleotide sequence.--

Please replace the paragraph beginning at page 6, line 20 with the following:

--**Figure 3. A.** Amino acid sequence of human and rat CLASP proteins. Sequences were aligned using ClustalW. One letter amino acid abbreviation used. Protein motifs are found within the labeled boxes. A "-" indicates gaps that are placed to acquire a best overall alignment. Other abbreviations: "HC2A" Human CLASP-2 sequence (SEQ ID NO:9), "KIAA" KIAA1058 sequence (SEQ ID NO:10) (Genbank Accession No. AB028981), "rat" TRG gene (SEQ ID NO:11) (Genbank Accession No. X68101), "HC4" Human CLASP-4 sequence (SEQ ID NO:12), "HC1" Human CLASP-1 sequence (SEQ ID NO:13), "HC3" Human CLASP-3 sequence (SEQ ID NO:14), "HC5" Human CLASP-5 sequence (SEQ ID NO:15). **B.** Alignment of DOCK motifs found within the human CLASPs (SEQ ID NOS:16-20, 24, 25, 27-31, 35, 37-43, 47 and 49-55) and rat TRG (SEQ ID NOS:26, 36 and 48) and compared to canonical DOCK motifs (SEQ ID NOS:21-23, 32-34, 44-46 and 56-58). Consensus amino acids found within all DOCK motifs are also indicated.--

Please replace the paragraph beginning at page 6, line 30 with the following:

sequence (SEQ ID NO:4) of CLASP-5 cDNA. Notable protein motifs are indicated. Additionally, boundaries between exons and introns are indicated by arrows. These

boundaries were defined by sequencing Bacterial Artificial Chromosomes containing genomic DNA corresponding to CLASP-5 (BACs). BACs were sequenced using primers derived from exon sequences corresponding to the CLASP-5 cDNA (SEQ ID NOS:59-63). Each exon/intron boundary is noted (as "Ref" with an appropriate reference number) above the cDNA sequence. The References contain exact nucleotide location of introns. The names and nucleotide numbers of the primers that were used in sequence reactions are also indicated. All nucleotide numbers refer to CLASP-5 cDNA sequence. As shown in the Reference, not all of the sequence from sequencing reactions produced sequence matching the cDNA. These nucleotide sequences that did not match the exon sequence for CLASP-5 were considered to be intron sequences. **B.** Alignment of human (SEQ ID NOS:9, 10 and 12-15) and rat (SEQ ID NO:11) CLASP amino acid sequences by ClustalW. Notable protein motifs are indicated. Additionally, the exon/intron borders described in part A are indicated with hand-drawn vertical lines between appropriate amino acids. Reference numbers are indicated in the right margin and correspond to References in part A.--

Please replace the paragraph beginning at page 8, line 10 with the following:

--**Figure 7.** Sequence of human CLASP-5 exons and introns, and promoter. **A)** Sequence of human CLASP-5 exons and intron borders (SEQ ID NOS:64-85). Stretches of noncontiguous genomic sequence from the Human Genome Project (Genbank entry gi10045359) were aligned using the human CLASP-5 cDNA as a template and Sequencher sequence analysis software. Due to the incompleteness of the Human Genome Project, only partial genomic sequence from human CLASP-5 was obtained. 22 exons representing approximately the 5' 40% of the human CLASP-5 cDNA sequence are shown. The sequence is aligned to the human CLASP-5 cDNA sequence. Nucleotide numbers in parentheses refer to the exon sequence within the uniquely-generated, contiguous

sequence having the isolated human CLASP-5 cDNA. Nucleotide numbers in parentheses refer to the exon sequence within the uniquely-generated, contiguous

gi10045359 sequence, which is located **7B**. **B)** Ordered stretch of human genomic DNA at the CLASP-5 locus (SEQ ID NO:86) aligned from noncontiguous, shotgun sequencing from the Human Genome Project using the human CLASP-5 sequence from FIG. 6A to determine genomic DNA fragment order and orientation. **C)** Sequence of putative human CLASP-5 promoter (SEQ ID NO:87). The 5' terminus of the CLASP-5 cDNA is underlined. This sequence represents nucleotides 126774 to 128870 of Genbank entry gi10045359.--

Please replace the paragraph beginning at page 8, line 27 with the following:

**--Figure 8.** Amino acid alignment and comparison between the human (h) CLASP family members (SEQ ID NO:88-93). Amino acid sequences were aligned using ClustalW. The alignment is presented in order of their greatest pairwise similarity scores. Single letter amino acid abbreviations are used. Astericks indicate complete identity, while colons and periods indicate sequence similarity among CLASP family members. Dashes indicate gaps inserted in the amino acid sequence to facilitate alignment. Labelled boxes are domains with similarity to known protein motifs; unlabelled boxes represent regions of similarity between all CLASPs and may represent CLASP-specific domains.--

Please replace the paragraph beginning at page 22, line 2 with the following:

--The CLASP-5 extracellular domain is characterized by one cadherin EC-like motif (Pigott, R. and Power, C., 1993, *The Adhesion Molecule Factbook*. Academic Press, pg. 6; Jackson, R. M. and Russell, R. B., 2000, *J. Mol. Biol.* 296: 325-34). Several highly conserved cysteines are found in the extracellular domain.

...in a homotypic and heterotypic manner to establish the immunological synapse in conjunction with molecules such as TCR, MHC class I, MHC class II, CD3 complex

and accessory molecules such as CD4, CD3, ICAM-1, LFA-1, and others. Many cadherins contain a pro-domain of approximately 50 to 150 amino acids that is removed before localization to the plasma membrane. This cleavage is presumed to be carried out by Furin (Posthaus, H. *et al.*, 1998, FEBS Let 438: 306-10) at a consensus sequence of RKQR (SEQ ID NO:6). Furin is a protease that is at least partially responsible for the maturation of certain cadherins. CLASP-5 contains the amino acid sequence RRTR (SEQ ID NO:7) encoded by the nucleotides 2770-2781.. By homology, this region is around 924 amino acids into the predicted protein start site for hCLASP-5 cDNA indicated in FIG. 6.--

Please replace the paragraph (**Table 1**) beginning at page 24, line 2 with the following:

--Table 1  
CLASP-5 ITAM Motifs

Motif No.	Sequence Motif	SEQ ID NO:
1	YXXV-X <sub>3</sub> -YXXV	8
2	YXXV-	-

Please replace the paragraph beginning at page 25, line 4 with the following:

--CLASP-5 polypeptides contain a new "DOCK" motif, not previously described in the scientific literature. The CLASP DOCK motif includes a series of five tyrosines surrounded by conserved sequences in regions A, B, C, D, and G (see FIG. 3B). There are also two highly conserved non-tyrosine containing regions (E and F) separated by 20 amino acids (P+EXAI+X+; SEQ ID NO:131) and (I+N(L)N(L)+GXV+DXXXXXXV; SEQ ID NO:132).

Please replace the paragraph beginning at page 52, line 9 with the following:

--In one embodiment, the antisense sequence is complementary to relatively accessible sequences of the CLASP-5 mRNA (*e.g.*, relatively devoid of secondary structure). This can be determined by analyzing predicted RNA secondary structures using, for example, the MFOLD program (Genetics Computer Group, Madison WI) and testing in vitro or in vivo as is known in the art. Another useful method for identifying effective antisense compositions uses combinatorial arrays of oligonucleotides (see, *e.g.*, Milner *et al.*, 1997, Nature Biotechnology 15: 537). Examples of oligonucleotides that can be tested in cells for antisense suppression of CLASP-5 function are those capable of hybridizing to (*i.e.*, substantially complementary to) CLASP-5 at the following positions:

Oligo	Sequence 5' - 3'	length	notes/comments
1	GATGTTGGAGCAGTAT CAGCATTCATA (SEQ ID NO:120)	27-mer	spans nucleotides 6-32 of the sequence of FIG. 1 (nucleotides 3087 to 3113 in FIG. 6)
2	GGGCAGCAGCCAGTTC TGTGAAGAGGAG (SEQ ID NO:121)	28-mer	spans nucleotides 154-181 of the sequence of FIG. 1 (nucleotides 3232 to 3259 in FIG. 6), and is complementary to the region encoding the cadherin EC motif
3	CAGCGGCGTGCACCA GGCACATGGCAGCC (SEQ ID NO:122)	29-mer	spans nucleotides 1650-1678 of the sequence of FIG. 1 (nucleotides 4728 to 4756 in FIG. 6), and is complementary to the region encoding the transmembrane domain

Please replace the paragraph beginning at page 53, line 4 with the following:

...can be made using any suitable method for producing a nucleic acid, such as the chemical synthesis and recombinant methods disclosed herein. In one embodiment, for

example, antisense RNA molecules of the invention can be prepared by de novo chemical synthesis or by cloning. For example, an antisense RNA that hybridizes to CLASP-5 mRNA can be made by inserting (ligating) an CLASP-5 DNA sequence (*e.g.*, SEQ ID NO:1, or fragment thereof) in reverse orientation operably linked to a promoter in a vector (*e.g.*, plasmid). Provided that the promoter and, preferably termination and polyadenylation signals, are properly positioned, the strand of the inserted sequence corresponding to the noncoding strand will be transcribed and act as an antisense oligonucleotide of the invention. The term "operably linked" refers to a functional linkage between a nucleic acid expression control sequence (such as a promoter or enhancer) and a second nucleic acid sequence, wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.--

Please replace the paragraph (Primer Table) beginning at page 107, line 20 with the following:

--Primer Table

CLASP gene	Sense Primer	Sense sequence	Sense SEQ ID NO:	Antisense Primer	Antisense sequence	Antisense SEQ ID NO:
CLASP-7	HC7gS5	AGGCCCTTGCTCTGTGTTA CCTG	123	HC7gAS1	TGTCATGTACTGCACCTCGCA CAGC	124
CLASP-7	HC7gS3	ACAGGAACCTGCTGTAC GTGTAC	125	HC7AS14	TGGTGGCTGCACAGGAATGG GGTG	126
CLASP-4	C4P2	GACCCATTAGGAGGTCT AC	127	HC4AS3'	CGGGATCCATTGTACCGTA CATCTGC	128
CLASP-4	C4P2	GACCCATTAGGAGGTCT AC	127	HC4AS3'	CGGGATCCATTGTACCGTA CATCTGC	128

AACT

AGATGAGATG

Please replace the paragraph beginning at page 108, line 1 with the following:

--In-frame stop codons were not present suggesting that the cDNA was not full length. To obtain the 5' terminus of CLASP-5, 5' RACE was employed. Antisense oligonucleotides directed against the 5' end of the longest CLASP-5 sequence were generated:

Primers used for human CLASP-5 5' RACE

Primer sequence(5' to 3')	nucleotide position
HC5RACE1 (SEQ ID NO:132)	
AAGGCAACTGGGAGACAGTAGGATCCAG	1838 to 1865
HC5RACE2 (SEQ ID NO:133)	
TGCTAGCATCTTCTCCACACATAAACTGG	1554 to 1582
HC5RACE3 (SEQ ID NO:134)	
AGGTGGTTGTCCTGGGTGTGTACAGAAG	1997 to 2012--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 142, at the end of the application.